



21-month old female with immunodeficiency and multiple autoimmunity

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Clinical Presentation

- Born in Brazil (minimal records), moved to US at 16 months (adopted)
- 4 months: persistent wheezing, possible pneumonia
- 5 months: low CD4 count (210 cells/ul) and IgG level (160 mg/dL)
started on Bactrim prophylaxis and IVIG
continued frequent respiratory infections in first year of life
- 14 months: x-ray proven pneumonia, requiring IV antibiotics
- 15 months: hospitalization for persistent diarrhea
stool positive for *C. diff* (PCR), improved on metronidazole
- 15-20 months: did well with appropriate weight gain - 50th percentile
- 21 months: admitted to our hospital for return of persistent diarrhea
treated for presumed *C. diff* without improvement
stool cultures were repeatedly negative
hemoglobin dropped to 6.2 g/dL (coombs-positive AIHA)

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- **Immune Labs:**

WBC: 12.4 kcells/uL
ANC: 5.8 kcells/uL
ALC: 5.5 kcells/uL

IgG: 691 mg/dL (IVIG)
IgM: 82 mg/dL
IgA: Undetectable
IgE: Undetectable

CD3+ 2018 cells/uL
CD3+4+ 627 cells/uL
CD3+8+ 1139 cells/uL
CD19+ 1988 cells/uL
CD16+56+ 945 cells/uL

IgD-CD27+ 0.3%
IgD+CD27+ 2.8%

CD4+CD45RA+CCR7+ 23.9%
CD8+CD45RA+CCR7+ 4.1%
CD8+CD45RA-CCR7- 41.4%
CD8+CD45RA+CCR7- 61.8%

Tregs: 2.5%
- Normal FOXP3 expression

Proliferation to Mitogens: Decreased
Proliferation to Antigens: Normal

Further Evaluation

- Peripheral blood positive for EBV on PRC (102,000 copies/mL).
- BAL showed neutrophilia and grew Klebsiella.
- Lung biopsy was significant for interstitial lymphoplasmacytic infiltrate with positive in situ hybridization for EBER.
- Endoscopy showed chronic active gastritis and colitis.
- GI biopsies were remarkable for loss of villi and absent goblet and Paneth cells consistent with autoimmune enteropathy in the stomach, small intestine, and colon.
- Linear staining along the periapical border of the enterocytes was positive for anti-enterocyte auto-antibody.

Diagnosis and Therapy

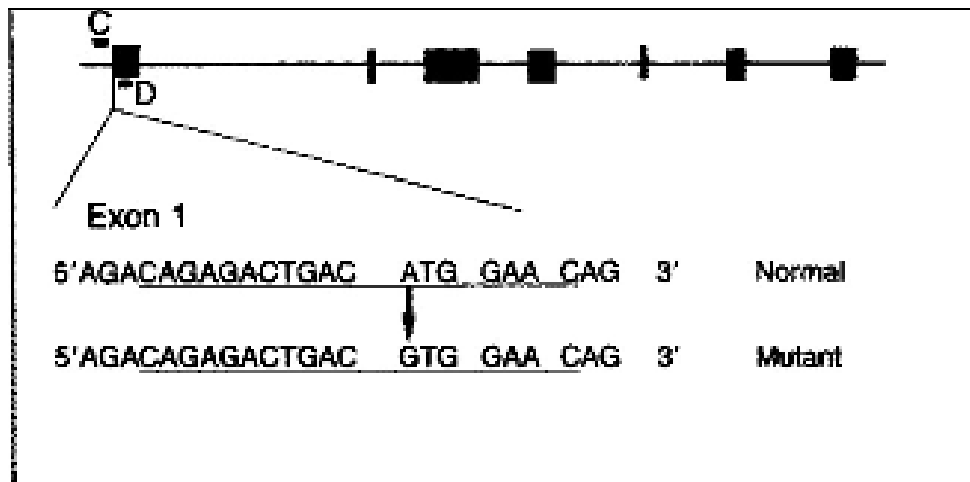
- 46-gene panel by massively parallel sequencing (BCM-NGS):

Homozygous for pathogenic variant in the CD3- γ gene (c.1A>G)

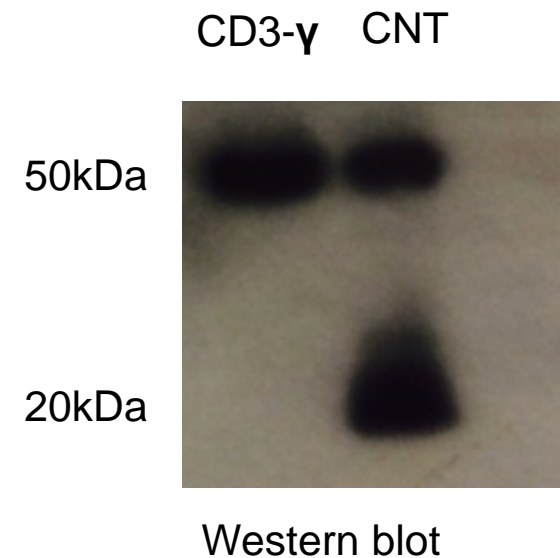
- Antibiotics started for Klebsiella infection in lungs.
- **Rituximab and Sirolimus** started for treatment of autoimmune hemolytic anemia, chronic lung disease, enteropathy, and EBV viremia.
- Continued on IVIG infusions.
- She had significant improvement in her clinical status.
- Scheduled to undergo HSCT from fully matched unrelated donor.

CD3- γ gene

- Chromosome 11, 7 exons.
- Encodes for CD3- γ polypeptide, which together with CD3- ϵ , - δ and - ζ , and the T-cell receptor alpha/beta and gamma/delta heterodimers, forms the T-cell receptor-CD3 complex.
- This complex plays an important role in coupling antigen recognition to several intracellular signal-transduction pathways.



Arnaiz-Villena A et al. N Engl J Med 1992



Thank you!

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